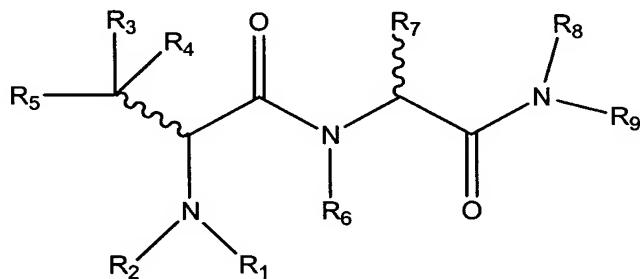


We claim:

1. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of a compound of Formula (II):



II

10

wherein:

- R₁ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

- R₂ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀,

-O₂CR₁₀, -SH, -SR₁₀, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-

5 R-;

or R₁ and R₂ taken together with the nitrogen atom to which they are attached is a three to seven membered ring;

10 R₃ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I,

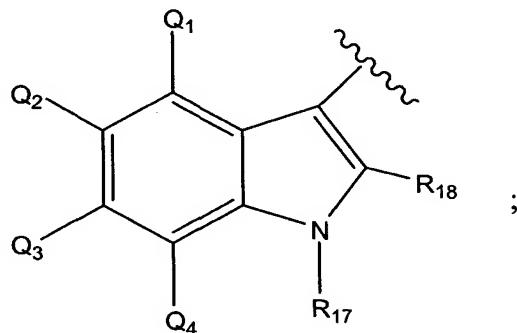
15 Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

20 R₄ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

25 30 or R₃ and R₄ taken together with the carbon to which they are attached form a three to seven membered ring;

R_5 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; aryl-R- and aryl and provided that when R₅ is an indolyl moiety of the formula

10



R_{17} is H or an optionally substituted alkyl or acyl group; and
 R_{18} , Q₁, Q₂, Q₃, and Q₄ are independently selected from H, halogen, alkyl, acyl, -OH, -O-alkyl, -O-acyl, -NH₂, -NH-alkyl, -N(alkyl)₂, -NH-acyl, -NO₂, -SH, -S-alkyl and -S-acyl, wherein the alkyl and acyl groups of the substituents are optionally substituted;

R_6 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

R₇ is selected from the group consisting of a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms,

5 said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-

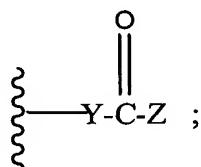
10 R- ;

R₈ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group;

15 and aryl-R-;

20

R₉ is:



25 and wherein,

R is a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂,

30

-NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group;

5

X is a moiety selected from the group consisting of: -OH, -OR, =O, =S, -O₂CR, -SH, -SR, -SO₂CR, -NH₂, -NHR, -N(R)₂, -NHCOR, -NRCOR, -I, -Br, -Cl, -F, -CN, -CO₂H, -CO₂R, -CHO, -COR, -CONH₂, -CONHR, -CON(R)₂, -COSH, -COSR, -NO₂, -SO₃H, -SOR, and -SO₂R;

10

Aryl is an aromatic ring selected from the group consisting of: phenyl, naphthyl, anthracyl, phenanthryl, thienyl, furyl, indolyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and pyridyl, optionally substituted with R or X;

15

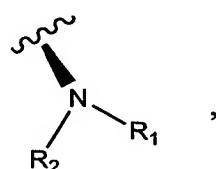
Y is a moiety selected from the group consisting of: a linear, saturated or unsaturated, one to six carbon alkyl group, optionally substituted with R, ArylR-, or X; and,

20

Z is a moiety selected from the group consisting of: -OH, -OR; -SH; -SR; -NH₂; -NHR; -N(R)₂; -NHCH(R₁₁)COOH; and -NRCH(R₁₁)COOH, wherein R₁₁ is a moiety having the formula: R, or -(CH₂)_nNR₁₂R₁₃, wherein n = 1-4 and R₁₂ and R₁₃ are independently selected from the group consisting of: H; R; and -C(NH)(NH₂);

25 with the provisos that:

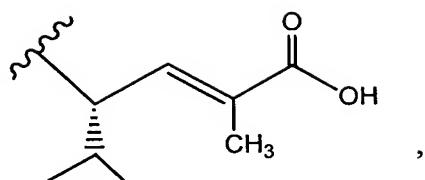
(1) when R₁ is H and R₂ is CH₃ of the moiety

30 R₃ is CH₃, R₄ is CH₃, R₅ is phenyl, R₆ is H, R₈ is CH₃,

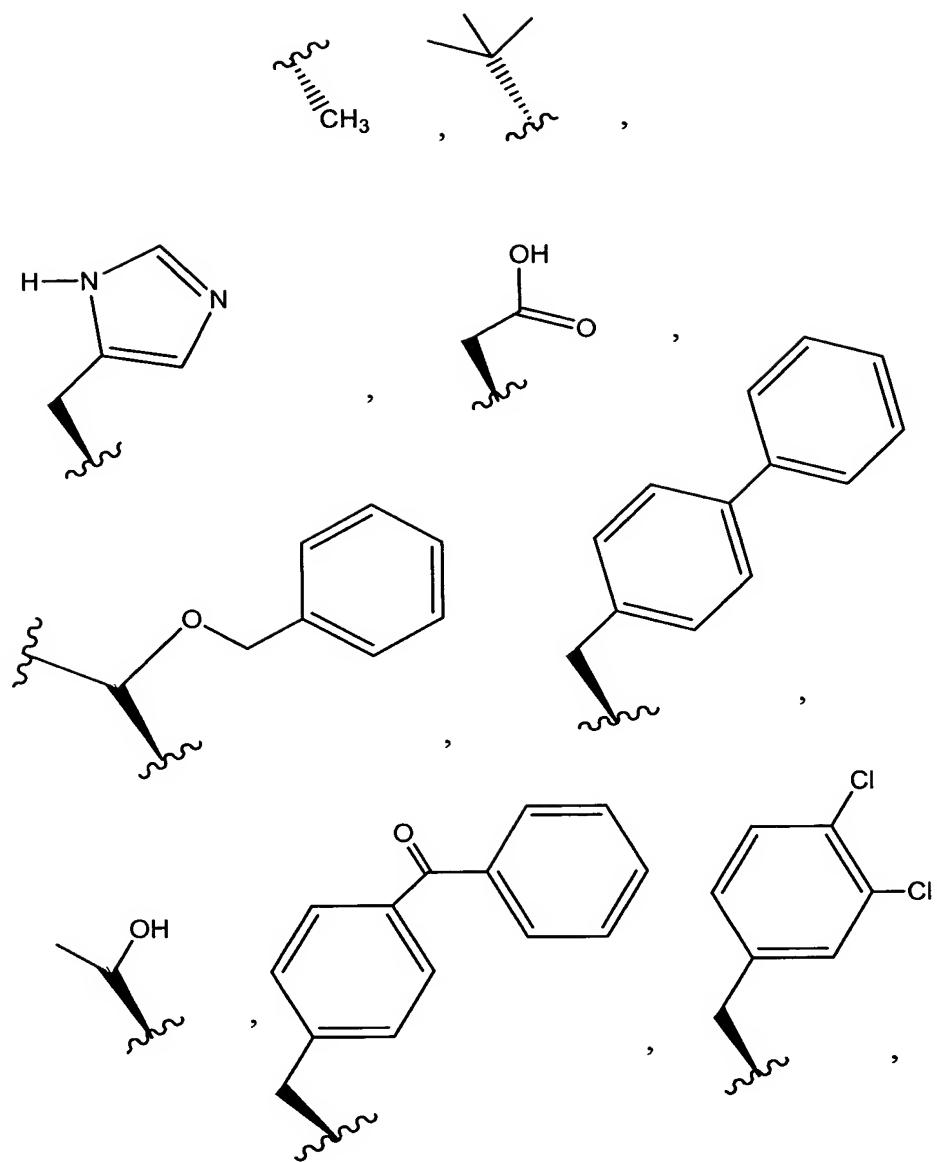
and

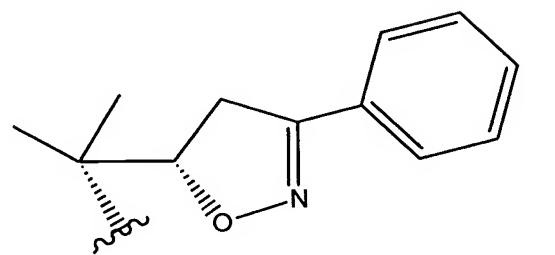
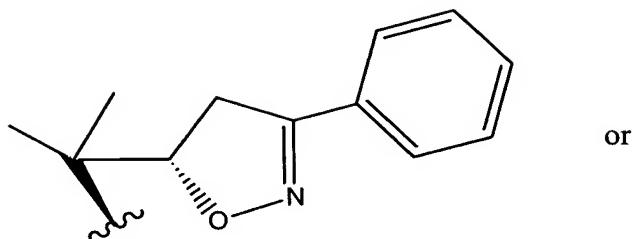
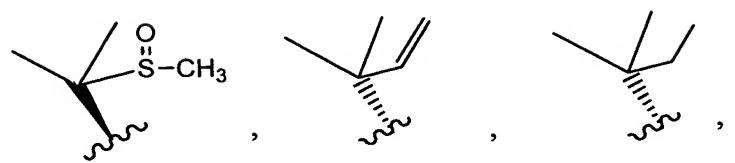
a) when R_9 is

5

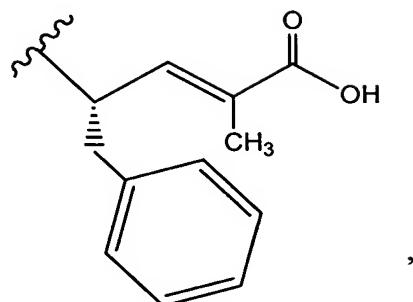


then R_7 is not





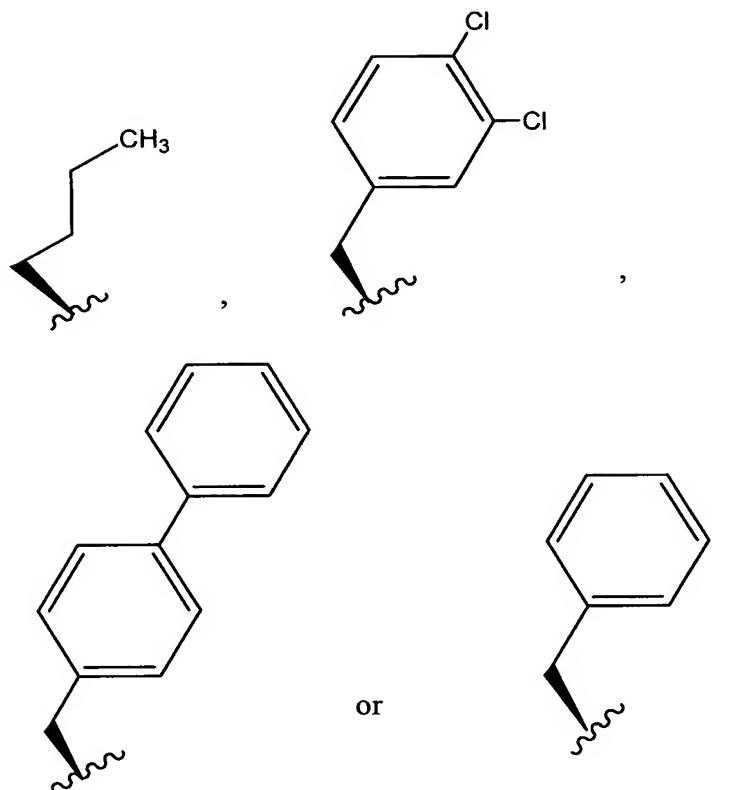
b) when R_9 is



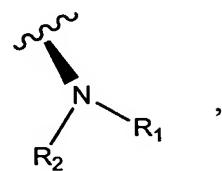
5

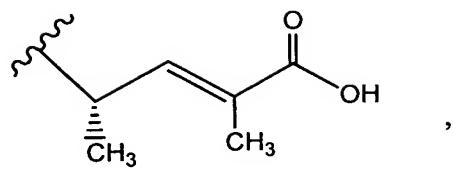
then R_7 is not

10



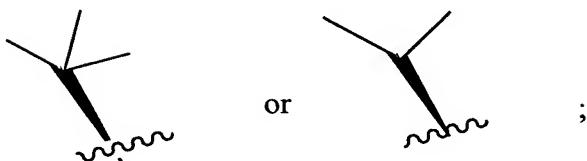
5

(2) when R₁ is H and R₂ is CH₃, of the moiety10 R₃ is CH₃, R₄ is CH₃, R₅ is phenyl, R₆ is H, R₈ is H,a) R₉ is



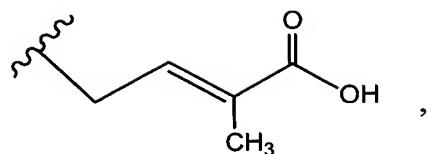
then R₇ is not

5



b) when R₉ is

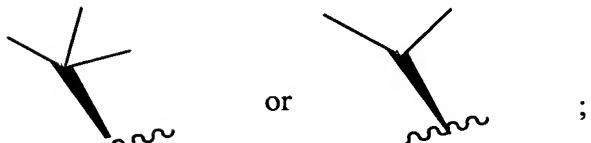
10



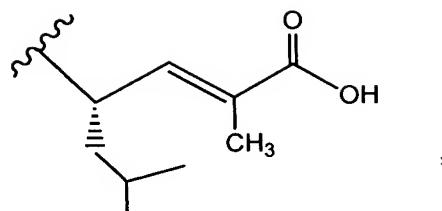
15

then R₇ is not

20

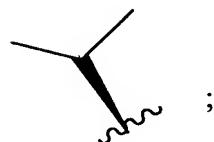


c) when R_9 is



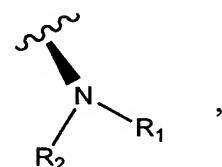
5

then R_7 is not



10

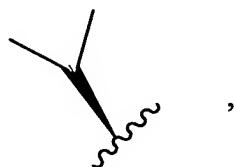
(3) when R_1 is H and R_2 is CH_3 , of the moiety



15

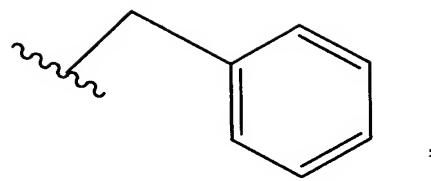
R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl, R_6 is H,

R_7 is



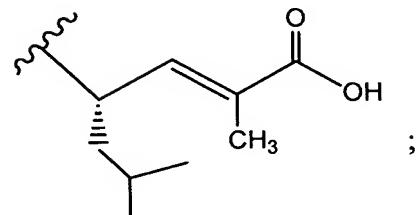
20

R_8 is



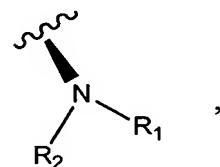
then R₉ is not

5



10

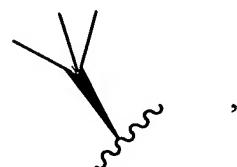
(4) when R₁ is H, R₂ is H, of the moiety



R₃ is CH₃, R₄ is CH₃, R₅ is phenyl, R₆ is H,

15

R₇ is

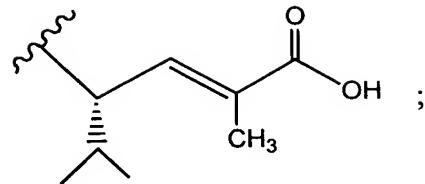


and

R₈ is CH₃,

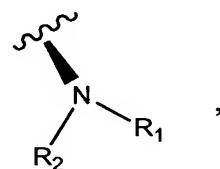
20

then R_9 is not



5

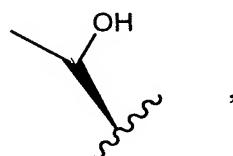
(5) when R_1 is H and R_2 is CH_3 of the moiety



R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl, R_6 is H,

10

R_7 is

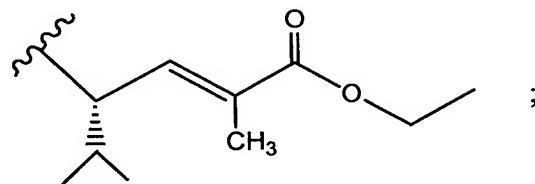


and

R_8 is CH_3 ,

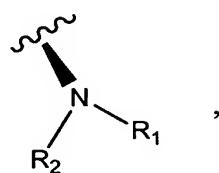
15

then R_9 is not



20

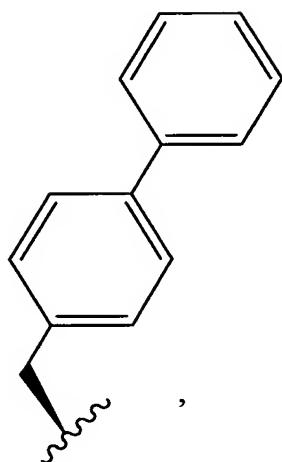
(6) when R₁ is H and R₂ is CH₃ of the moiety



R₃ is CH₃, R₄ is CH₃, R₅ is phenyl, R₆ is H,

5

R₇ is



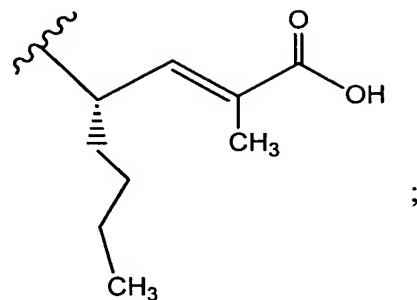
and

R₈ is CH₃,

10

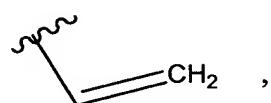
then R₉ is not

15



(7) when R_1 is H, R_2 is H, R_3 is CH_3 , R_4 is CH_3 , R_5 is

5

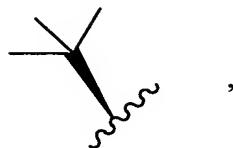


R_6 is H,

R_7 is

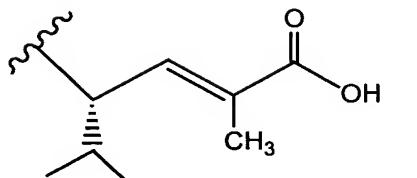
10

and



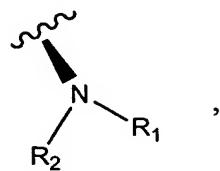
R_8 is CH_3 ,

15 then R_9 is not



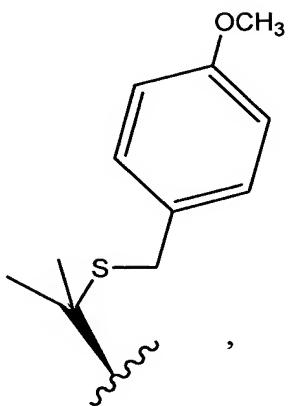
20

(8) when R_1 is H and R_2 is CH_3 , of the moiety



5 R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl, R_6 is H,

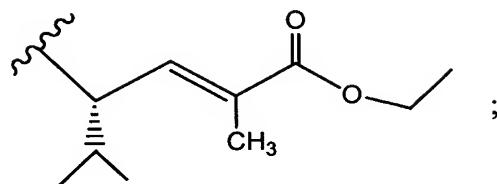
R_7 is



and

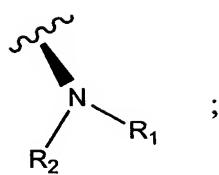
10 R_8 is CH_3 ,

then R_9 is not



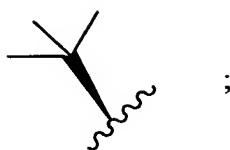
15

(9) when R_1 is H and R_2 is CH_3 of the moiety



R₃ is CH₃, R₄ is CH₃, R₅ is phenyl,
R₆ is H,

5 R₇ is

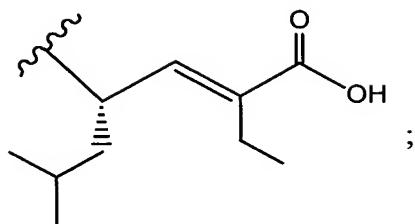


and

R₈ is H,

10 then R₉ is not

15



(10) when R₁ is H, R₂ is CH₃,

20

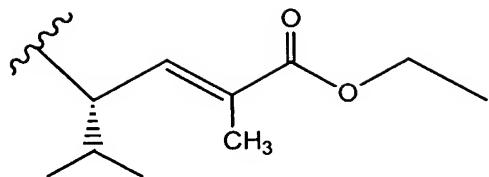
R₃ is H, R₄ is phenyl, R₅ is phenyl,
R₆ is H,

R_8 is CH_3 ,

and

R_9 is

5



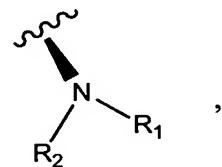
10

then R_7 is not



15

(11) when R_1 is H and R_2 is CH_3 of the moiety



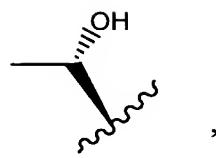
R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl,

20 R_6 is H,

R_8 is CH_3 ,

and

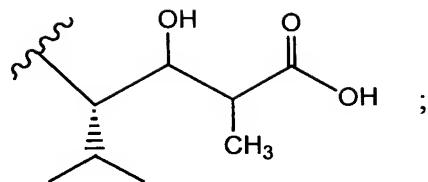
R_7 is



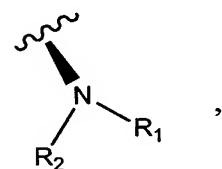
5

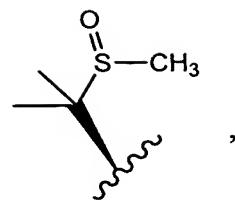
then R₉ is not

10



15

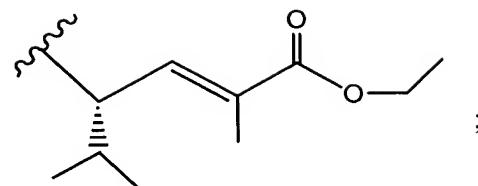
(12) when R₁ is H and R₂ is CH₃ of the moietyR₃ is CH₃, R₄ is CH₃, R₅ is phenyl,20 R₆ is H,R₇ is



and

R_8 is CH_3 ,

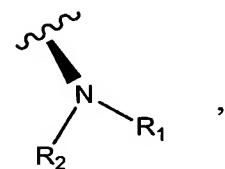
5 then R_9 is not



10

15

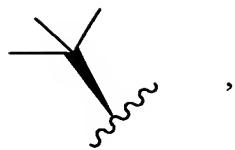
(13) when R_1 is H and R_2 is CH_3 of the moiety



R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl,

20 R_6 is H,

R_7 is



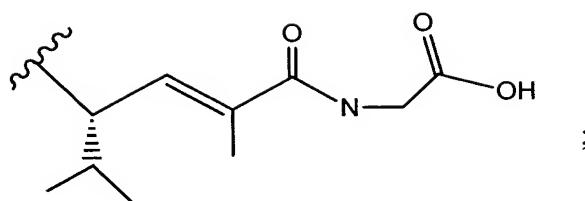
and

R_8 is CH_3 ,

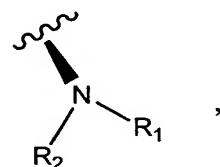
5

then R_9 is not

10



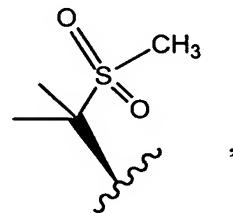
(14) when R_1 is H and R_2 is CH_3 of the moiety



15 R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl,

R_6 is H,

R_7 is

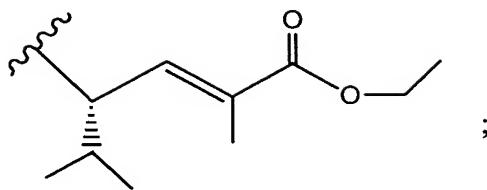


20 and

R_8 is CH_3 ,

then R_9 is not

5



10

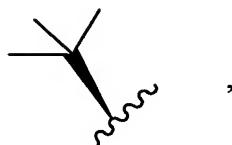
(15) when R_1 is CH_3 , R_2 is H ,

R_3 is H , R_4 is phenyl, R_5 is phenyl,

R_6 is H ,

15

R_7 is



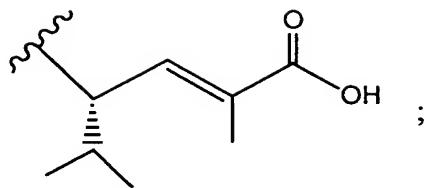
and

R_8 is CH_3 ,

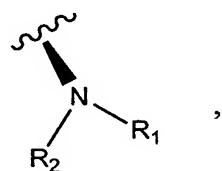
20

then R_9 is not

25



5 (16) when R₁ is CH₃ and R₂ is H of the moiety

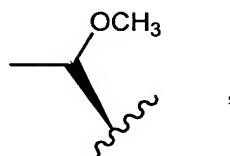


R₃ is CH₃, R₄ is methyl, R₅ is phenyl,

R₆ is H,

10

R₇ is

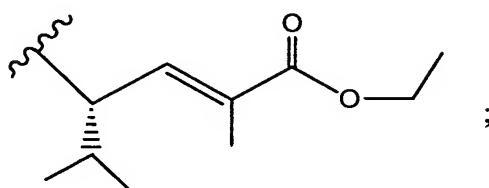


and

R₈ is CH₃,

15

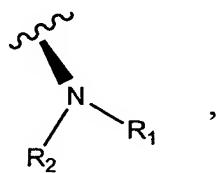
then R₉ is not



20

(17) when R₁ is CH₃ and R₂ is H of the moiety

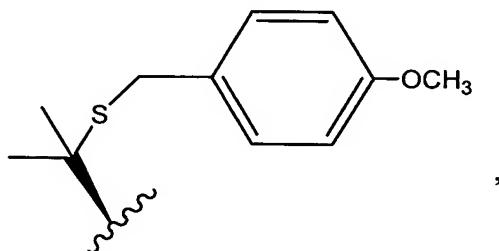
5



R₃ is CH₃, R₄ is methyl, R₅ is 4-methoxyphenyl,
R₆ is H,

R₇ is

10

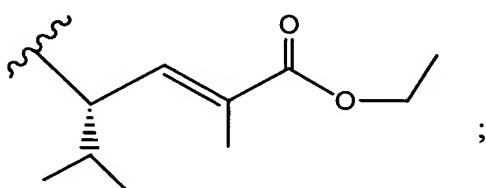


and

R₈ is CH₃,

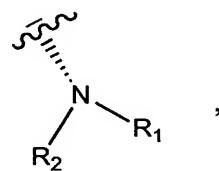
then R₉ is not

15



20

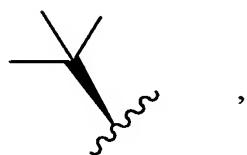
(18) when R₁ is CH₃ and R₂ is H of the moiety



R₃ is CH₃, R₄ is CH₃, R₅ is 3-chlorophenyl,

5 R₆ is H,

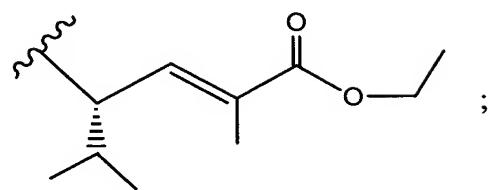
R₇ is



and

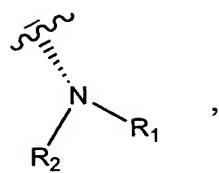
10 R₈ is CH₃,

then R₉ is not



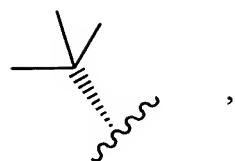
15

20 (19) when R₁ is CH₃ and R₂ is H of the moiety



R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl,
 R_6 is H,

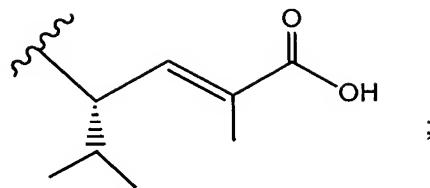
5 R_7 is



and

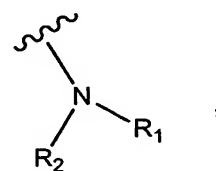
R_8 is CH_3 ,

10 then R_9 is not



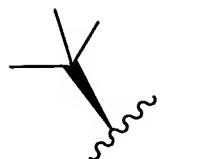
15

(20) when R_1 is CH_3 and R_2 is CH_3 of the moiety



20 R_3 is H, R_4 is H, R_5 is 3-pyridyl,
 R_6 is H,

R_7 is

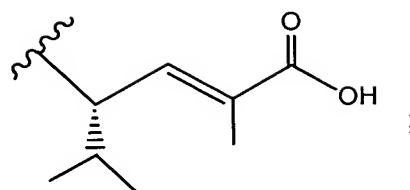


and

5 R_8 is CH_3 ,

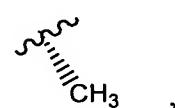
then R_9 is not

10



15

(21) when R_1 is CH_3 and R_2 is H , R_3 is

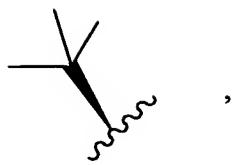


20

R_4 is H , R_5 is $-O-CH_2$ -phenyl,

R_6 is H ,

R_7 is

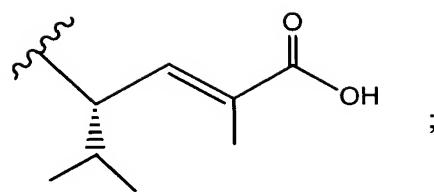


and

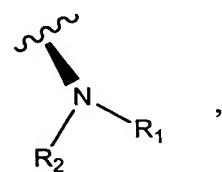
R_8 is CH_3 ,

5 then R_9 is not

10



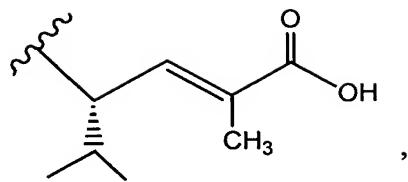
15 (22) when R_1 is H and R_2 is CH_3 of the moiety



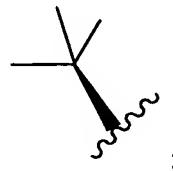
R_3 is CH_3 , R_4 is CH_3 , R_5 is phenyl, R_6 is CH_3 , R_8 is CH_3 ,

and

20 R_9 is



then R₇ is not



(23) when R₁ is H;

5

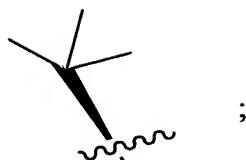
R₃ and R₄ are CH₃;

R₅ is phenyl;

10

R₆ is H;

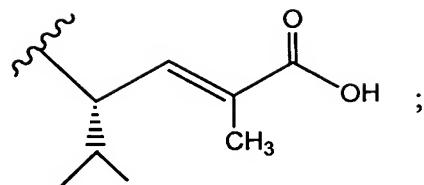
R₇ is



15

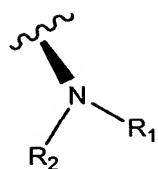
R₈ is CH₃;

R₉ is



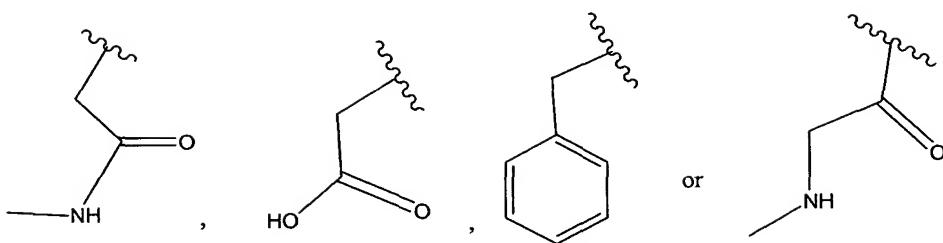
20

then R₂ of the moiety



5

is not



10

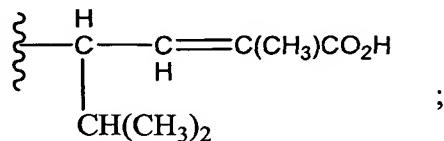
or pharmaceutically acceptable salts thereof.

- 15 2. The method according to Claim 1 wherein the chemotherapeutic agents are antimicrotubule inhibitors.
3. The method according to Claim 2 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine
20 and vinorelbine.
4. The method according to claim 1 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia, kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

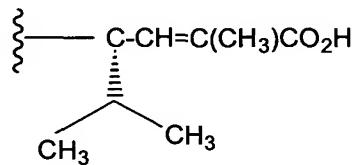
25

5. The method according to Claim 1 wherein the tumors overexpress MDR-1, MXR or MRP.
 6. The method according to Claim 1 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).
 7. The method according to Claim 1 wherein the resistance is inherent or acquired.
 8. The method according to Claim 7 wherein the resistance is acquired.
- 10
9. The method according to Claim 1 wherein a compound of Formula (II) is administered before, concurrently, or after treatment with the chemotherapeutic agent.
- 15 10. The method according to Claim 1 wherein:
- (a) R₁ and R₂ are independently: H, methyl, ethyl, propyl, or n-butyl; or
 - (b) R₁ and R₂ taken together with the nitrogen atom to which they are attached form a three to six membered ring;
11. The method according to Claim 10 wherein R₁ and R₂ are independently: H or
- 20 CH₃.
12. The method according to Claim 11 wherein R₁ is H and R₂ is CH₃.
13. The method according to Claim 10 wherein no more than one of R₁ and R₂ is H.
14. The method according to Claim 1 wherein R₃ and R₄ are independently: H,
- 25 methyl, ethyl, n-propyl or n-butyl, provided no more than one of R₃ and R₄ is H or, R₃ and R₄ are joined to form a β-cyclopropyl, β-cyclobutyl, β-cyclopentyl or β-cyclohexyl ring.
15. The method according to Claim 14 wherein R₃ and R₄ are each methyl.
16. The method according to Claim 1 wherein R₅ is cyclohexyl, phenyl, naphthyl,
- 30 thienyl, anthracyl, pyrrolyl or indolyl.

17. The method according to Claim 16 wherein R₅ is phenyl, or indolyl.
18. The method according to Claim 17 wherein R₅ is phenyl;
19. The method according to Claim 1 wherein R₆ and R₈ are independently: H or methyl.
- 5 20. The method according to Claim 19 wherein R₆ is H and R₈ is methyl.
21. The method according to Claim 1 wherein R₇ is a three to six carbon, branched alkyl group.
22. The method of Claim 21 where R₇ is -C(CH₃)₃.
23. The method of Claim 1 wherein; Z is OH, or -OR₁₄; R₁₄, is a linear or branched one to six carbon alkyl group, -NHCH(R)₁₁)COOH or -NCH₃CH(R₁₁)COOH; R₁₁ is R, or - (CH₂)_n NHC (NH) (NH₂) ; or
- 10 R₉ is -C(R₁₅)-C=C(R₁₆)C(O)-OH wherein R₁₅ is methyl, ethyl, n-propyl, isopropyl, tert-butyl, iso-butyl, or sec-butyl and R₁₆ is H, methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl or sec-butyl.
- 15 24. The method according to claim 1 wherein R₉ is:

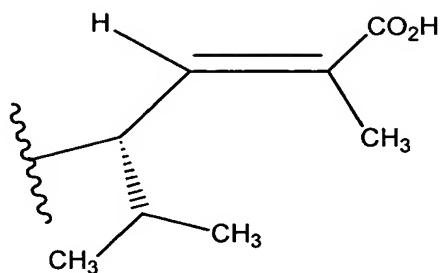


25. The method according to Claim 1 wherein
- 20 R₉ is

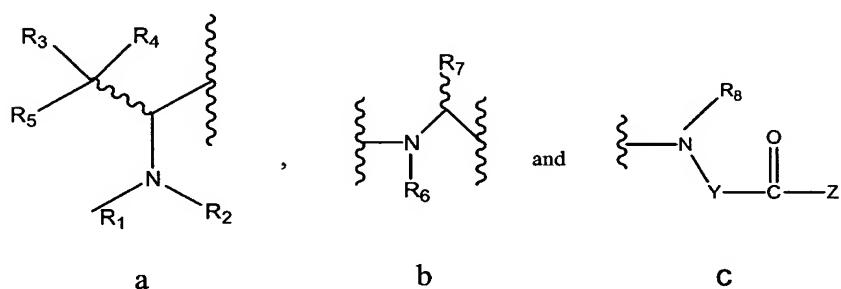


26. The method according to Claim 1 wherein R₉ is:

5



10 27. The method according to Claim 1 wherein the absolute configurations of
moieties a, b and c of Formula (II) are:



15 are selected from:

<u>a</u>	<u>b</u>	<u>c</u>
S	S	S
R	S	S
and S	S	R.

20

28. The method according to claim 1 wherein said compound of Formula (II) is selected from:

3-Chloro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide ,

5 4-Chloro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

4-chloro-N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

10 4-Chloro-N, β,β -triethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

4-Chloro-N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

15 N, $\beta,\beta,3$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

20 N, $\beta,\beta,3$ -tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N, $\beta,\beta,3$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

25 N, $\beta,\beta,3$ -Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N, $\beta,\beta,4$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

30 N, $\beta,\beta,4$ -tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

- N, β , β ,4-Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 5 N, β , β ,4-Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- N, β , β ,3,4-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 10 N, β , β ,3,4-pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- N, β , β ,3,4-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 15 N, β , β ,3,4-Pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- N, β , β ,3,4-Pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 20 N, β , β ,3,5-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- N, β , β ,3,5-pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 25 N, β , β ,3,5-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- N, β , β ,3,5-Pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 30 N-Methyl-3-(2-thienyl)-L-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N-methyl-3-(2-thienyl)-D-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,

- 5 N-Methyl-3-(2-thienyl)-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

N-Methyl-3-(2-thienyl)-D-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

- 10 N-Methyl-3-thien-3-yl-L-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N¹,3-dimethyl-L-valinamide,

- 15 N-methyl-3-thien-3-yl-D-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N-Methyl-3-thien-3-yl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

- 20 N-Methyl-3-thien-3-yl-D-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

3-(1-Benzothien-3-yl)-N-methylvalyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

- 25 3-(1-Benzothien-3-yl)-N-methylvalyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

- 30 3-(1-Benzothien-2-yl)-N-methylvalyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

3-(1-Benzothien-2-yl)-N-methylvalyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

4-tert-Butyl-N, β,β -trimethylphenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

5 4-tert-Butyl-N, β,β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N-Ethyl- β,β -dimethylphenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

10 N-Ethyl- β,β -dimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

15 N-(tert-Butoxycarbonyl)-N- β,β ,2-tetramethylphenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N, β,β ,2-tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

20 N, β,β ,2-Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N, β,β ,2-Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

25 N, β,β ,2-Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

30 3-bromo-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

- 3-bromo-N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 5 3-phenyl-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 10 3-phenyl-N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 15 3-ethyl- N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 20 4-bromo-N, β,β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 25 4-phenyl-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 30 4-carboxy-N, β,β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 35 3-Hydroxy-N, β,β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 40 N,3-Dimethyl-4-phenyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N,3-dimethyl-4-phenyl-D-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

5 (2E,4S)-4-[((2S)-2-{[(2S)-3,3-dimethyl-2-(methylamino)octanoyl]amino}-3,3-dimethylbutanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

(2E,4S)-4-[((2S)-2-{[(2R)-3,3-dimethyl-2-(methylamino)octanoyl]amino}-3,3-dimethylbutanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

10 N,N, β -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N-(2-hydroxyethyl)-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

15 2-Methoxy-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

20 2-Methoxy-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

25 N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

2-Methoxy-N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

30 2-Methoxy-N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

3-Fluoro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

5 3-Fluoro- N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2- butenyl]-N¹,3-dimethyl-L-valinamide,

N, β,β -Trimethyl-3-(trifluoromethyl)-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

10 N, β,β -Trimethyl-3-(trifluoromethyl)-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

15 3,5-Difluoro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

15 3,5-Difluoro-N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

20 N, β,β -trimethyl-3,5-bis(trifluoromethyl)-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N, β,β -trimethyl-3,5-bis(trifluoromethyl)-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

25 O-isopropyl-N, β,β -trimethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

O-isopropyl- N, β,β -trimethyl-D-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

30

- 3-Cyclohexyl-N-methyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 5 (2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid,
- (2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid,
- 10 (2E,4R)-2,5-dimethyl-4-(methyl{3-methyl-N-[(methylamino)(1-phenylcyclohexyl)acetyl]-L-valyl}amino)-2-hexenoic acid,
- (E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-phenylpropanoyl)amino]-2-hexenoic acid,
- 15 N, β , β -Trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-butyl-3-carboxybut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- N, β , β -Trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isobutyl-2-pentenyl]-N¹,3-dimethyl-L-valinamide,
- 20 (E,4S)-2-Butyl-4-[((2S)-3,3-dimethyl-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)amino]-5-methyl-2-hexenoic acid,
- 25 N, β , β -Trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-pentenyl]-N¹,3-dimethyl-L-valinamide,
- Ethyl (E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-(methylsulfanyl)butanoyl]amino}-2-hexenoate,
- 30 (E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-(methylsulfanyl)butanoyl]amino}-2-hexenoic acid,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-3-(methylsulfonyl)-L-valinamide,

5 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-3-[(4-methoxybenzyl)sulfanyl]-N¹-methyl-L-valinamide,

N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-3-[(4-methoxybenzyl)sulfanyl]-N¹-methyl-L-valinamide,

10 N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-3-(methylsulfonyl)-L-valinamide,

15 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1R,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹-methyl-L-allothreoninamide,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-allothreoninamide,

20 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N,O, β , β -tetramethyl-L-tyrosinamide,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,O-dimethyl-L-allothreoninamide,

25 (E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino)-4-phenylbutanoyl]amino]-2-hexenoic acid,

30 N, β , β -trimethyl-L-phenylalanyl-4-benzoyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]- N, β , β -trimethyl-L-phenylalaninamide,

4-benzoyl-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

5 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-N¹-methyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-3-methyl-L-valinamide,

10 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-ethyl-3-methyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-ethyl-L-valinamide,

15

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-methyl-L-leucinamide,

20

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-methyl-L-norvalinamide,

(2E,4S)-4-[(2R)-2-cyclohexyl-2-[(N, β,β -trimethyl-L-phenylalanyl)amino]ethanoyl}(methyl)amino]-2,5-dimethylhex-2-enoic acid,

25

(2E,4S)-2,5-dimethyl-4-(methyl{(2S)-2-[(N, β,β -trimethyl-L-phenylalanyl)amino]butanoyl}amino)hex-2-enoic acid,

4-{{[3,3-Dimethyl-2-(2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino}-2,5-dimethyl-hex-2-enoic acid,

30

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-methyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-L-valinamide,

5 2,5-dimethyl-4-{methyl-[2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-propionyl]-amino}-hex-2-enoic acid,

4-{{[3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino}-2,6-dimethyl-hept-2-enoic acid,

10 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-isoleucinamide,

15 (E,4S)-4-[((2S)-3,3-dimethyl-2-{{(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl}(methyl)amino]-2,5-dimethyl-2-hexenamide,

(E,4S)-4-[((2S)-3,3-dimethyl-2-{{(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl}(methyl)amino]-N,2,5-trimethyl-2-hexenamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(2-cyanoethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-but enyl}-N¹,3-dimethyl-L-valinamide,

25 N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(carboxymethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-but enyl}-N¹,3-dimethyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(4-azidophenyl)amino]-1-isopropyl-3-methyl-4-oxo-2-but enyl}-N¹,3-dimethyl-L-valinamide,

30 N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-[(2-phenylethyl)amino]but-2-enyl}-N¹,3-dimethyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl](methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl}-N¹-,3-dimethyl-L-valinamide,

5 N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl](methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl}-N-1-,3-dimethyl-L-valinamide,

10 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-(thien-2-ylmethoxy)but-2-enyl]-N¹-,3-dimethyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-isopropyl-3-methyl-4-(octyloxy)-4-oxobut-2-enyl]-N¹-,3-dimethyl-L-valinamide,

15 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2Z)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylprop-2-enyl]-N¹,3-dimethyl-L-valinamide,

20 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-allyl-3-carboxybut-2-enyl]-N¹,3-dimethyl-L-valinamide,

25 (2E,4S)-4-[(2S)-3,3-dimethyl-2-[(N, β,β -trimethyl-L-phenylalanyl)amino]-4-pentenoyl](methyl)amino]-2,5-dimethyl-2-hexenoic acid,

(2E, 4S)-4-[((2S)-2-{[3,3-dimethyl-2-(methylamino)-4-pentenoyl]amino}-3,3-dimethylbutanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

30 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-isoleucinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1R,3S)-3-carboxy-1-isopropylbutyl]-N^{1,3}-dimethyl-L-valinamide,

5 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1R,3R)-3-carboxy-1-isopropylbutyl]-N^{1,3}-dimethyl-L-valinamide,

β,β -diethyl-N-methyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,

10 β,β -diethyl-N-methyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,

15 β,β -dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,

O-benzyl-N-methyl-L-threonyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,

20 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,

(2E,4S)-4-[((2S)-2-{[(2S)-2-Amino-3-(1-naphthyl)propanoyl]amino}-3,3-dimethylbutanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

25 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-methyl-D-valinamide,

(E,4S)-4-[((2S)-3,3-dimethyl-2-{[(2S)-3-methyl-2-(methylamino)-3-(1-methyl-1H-ethyl-1H-indol-3-yl)butanoyl]amino}butanoyl)amino]-2,5-dimethyl-2-hexenoic acid,

30 ethyl (E,4S)-4-[((2S)-3,3-dimethyl-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoate,

- (E,4S)-4-[((2S)-3,3-dimethyl-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,
- Ethyl (E,4S)-4-[((2S)-3,3-dimethyl-2-{[(2R)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoate,
5 (E,4S)-4-[((2S)-3,3-dimethyl-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)(methyl)amino]-2-methyl-5-phenyl-2-pentenoic acid,
- (E,4S)-2,5-dimethyl-4-[methyl((2S)-2-{[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-phenylpropanoyl)amino]-2-hexenoic acid,
10 (4R)-4-[((2S)-2-{[(2S)-2-amino-4-methylpentanoyl]amino}-3,3-dimethylbutanoyl)amino]-2,5-dimethylhexanoic acid,
15 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-alpha-glutamine,
N,3-dimethyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
20 N, β , β -trimethyl-L-tryptophyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
25 3-cyclohexyl-N-methyl-L-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,
30 (2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

2-(4-{[3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino}-2,5-dimethyl-hex-2-enoylamino)-4-methylsulfanyl-butyric acid methyl ester,

5 N, β , β -trimethyl-L-phenylalanyl-N1-((1S,2E)-4-{{(1S)-1-carboxy-3-(methylthio)propyl]amino}-1-isopropyl-3-methyl-4-oxobut-2-enyl)-N1,3-dimethyl-L-valinamide,

10 N, β , β -trimethyl-4-[(E)-2-phenylvinyl]-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N, β , β -trimethyl-4-[(E)-2-phenylvinyl]-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

15 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2'enyl]-3-fluoro-N¹-methyl-D-valinamide,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N¹-methyl-L-valinamide,

20 3-[(4-methoxybenzyl)thio]-N-methyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

25 N-ethyl- β , β -dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-3-methyl-3-phenyl-2-pyrrolidin-1-ylbutanoyl]-L-valyl}amino)hex-2-enoic acid,

30 N-(2-hydroxyethyl)- β , β -dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

(β R)-N, β -dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

5 3-acetyl-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-hydroxy-N¹-methyl-L-valinamide, and

10 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1R,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

29. The method according to claim 28 wherein said compound of Formula (II) is
15 selected from:
3-Chloro-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide ,

4-Chloro- N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-
20 4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

4-chloro- N, β , β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

25 4-Chloro- N, β , β -triethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

4-Chloro-N, β , β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide and

30 3-ethyl- N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide or pharmaceutically acceptable salts thereof.

30. The method according to Claim 28 wherein said compound of Formula (II) is selected from:

- 5 N, $\beta,\beta,3$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- N, $\beta,\beta,3$ -tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 10 N, $\beta,\beta,3$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- N, $\beta,\beta,3$ -Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 15 N, $\beta,\beta,4$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- N, $\beta,\beta,4$ -Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 20 N, $\beta,\beta,4$ -tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- N, $\beta,\beta,4$ -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 25 N, $\beta,\beta,4$ -Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- N, $\beta,\beta,3,4$ -Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 30 N, $\beta,\beta,3,4$ -pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N, β , β ,3,4-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

5 N, β , β ,3,4-Pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

N, β , β ,3,5-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,

10

N, β , β ,3,5-pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,

15

N, β , β ,3,5-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide and

N, β , β ,3,5-Pentamethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide

or pharmaceutically acceptable salts thereof.

20

31. The method according to claim 28 wherein said compound of Formula (II) is selected from:

25

N-Methyl-3-(2-thienyl)-L-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,

N-methyl-3-(2-thienyl)-D-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,

30

N-Methyl-3-(2-thienyl)-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

N-Methyl-3-(2-thienyl)-D-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-buteny]-N¹,3-dimethyl-L-valinamide,

5 N-Methyl-3-thien-3-yl-L-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N-methyl-3-thien-3-yl-D-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl]-N¹,3-dimethyl-L-valinamide,

10 N-Methyl-3-thien-3-yl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide and

N-Methyl-3-thien-3-yl-D-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide

15 or pharmaceutically acceptable salts thereof.

32. The method according to claim 28 wherein said compound of Formula (II) is selected from:

20 3-(1-Benzothien-3-yl)-N-methylvalyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-buteny]-N¹,3-dimethyl-L-valinamide,

3-(1-Benzothien-3-yl)-N-methylvalyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-buteny]-N¹,3-dimethyl-L-valinamide,

25 3-(1-Benzothien-2-yl)-N-methylvalyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-buteny]-N¹,3-dimethyl-L-valinamide and

30 3-(1-Benzothien-2-yl)-N-methylvalyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-buteny]-N¹,3-dimethyl-L-valinamide

or pharmaceutically acceptable salts thereof.

33. The method according to Claim 28 wherein said compound of Formula (II) is selected from:

- 5 4-tert-Butyl-N, β , β -trimethylphenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 10 4-tert-Butyl-N, β , β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,
- 15 N-Ethyl- β , β -dimethylphenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide and
N-Ethyl- β , β -dimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide
20 or pharmaceutically acceptable salts thereof.

34. The method according to claim 28 wherein said compound of Formula (II) is selected from:

- 20 N-(tert-Butoxycarbonyl)-N- β , β ,2-tetramethylphenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
N, β , β ,2-tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
25 N, β , β ,2-Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,
N, β , β ,2-Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide and
30 N¹,3-dimethyl-L-valinamide and

N, β , β ,2-Tetramethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

- 5 35. The method according to claim 28 wherein said compound of Formula (II) is selected from:

3-bromo-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

- 10 3-bromo-N, β , β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide and

- 15 4-bromo-N, β , β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

36. The method according to claim 28 wherein said compound of Formula (II) is selected from:

- 20 3-phenyl-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

- 25 3-phenyl-N, β , β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide and

- 4-phenyl-N, β , β --trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

- 30 37. The method according to claim 28 wherein said compound of Formula (II) is selected from:

4-carboxy- N, β , β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

5 3-Methoxy- N, β , β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide and

3-Hydroxy- N, β , β -trimethylphenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide

10 or pharmaceutically acceptable salts thereof.

38. The method according to claim 28 wherein said compound of Formula (II) is selected from:

15 N, β , β -trimethyl-3-vinyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N,3-Dimethyl-4-phenyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

20 N,3-dimethyl-4-phenyl-D-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

(2E,4S)-4-[((2S)-2-{[(2S)-3,3-dimethyl-2-(methylamino)octanoyl]amino}-3,3-dimethylbutanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

(2E,4S)-4-[((2S)-2-{[(2R)-3,3-dimethyl-2-(methylamino)octanoyl]amino}-3,3-dimethylbutanoyl)(methyl)amino]-2,5-dimethyl-2-hexenoic acid,

30 N,N, β , β -Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide and

N-(2-hydroxyethyl)-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

- 5 39. The method according to claim 28 wherein said compound of Formula (II) is selected from:

2-Methoxy-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

10

2-Methoxy-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

15

N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

20

2-Methoxy-N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹,3-dimethyl-L-valinamide,

2-Methoxy-N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide,

25

O-isopropyl- N, β , β -trimethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide and

30

O-isopropyl- N, β , β -trimethyl-D-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide

or pharmaceutically acceptable salts thereof.

40. The method according to claim 28 wherein said compound of Formula (II) is selected from:

5 3-Fluoro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

3-Fluoro- N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

10 N, β,β -Trimethyl-3-(trifluoromethyl)-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

N, β,β -Trimethyl-3-(trifluoromethyl)-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

15 3,5-Difluoro- N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

20 3,5-Difluoro- N, β,β -trimethyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N, β,β -trimethyl-3,5-bis(trifluoromethyl)-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide and

25 N, β,β -trimethyl-3,5-bis(trifluoromethyl)-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

41. The method according to claim 28 wherein said compound of Formula (II) is
30 selected from:

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1-phenylcyclopentyl)ethanoyl]-L-valyl}amino)-2-hexenoic acid and

- 5 (2E,4R)-2,5-dimethyl-4-(methyl{3-methyl-N-[(methylamino)(1-phenylcyclohexyl)acetyl]-L-valyl}amino)-2-hexenoic acid
or pharmaceutically acceptable salts thereof.

42. The method according to claim 28 wherein said compound of Formula (II) is
10 selected from:

(E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino)-3-phenylpropanoyl]amino]-2-hexenoic acid,

- 15 N, β , β -Trimethyl-L-phenylalanyl- N^1 -[(1S,2E)-1-butyl-3-carboxybut-2-enyl]- N^1 ,3-dimethyl-L-valinamide,

N, β , β -Trimethyl-L-phenylalanyl- N^1 -[(1S,2E)-3-carboxy-1-isobutyl-2-pentenyl]- N^1 ,3-dimethyl-L-valinamide,

- 20 (E,4S)-2-Butyl-4-[((2S)-3,3-dimethyl-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)amino]-5-methyl-2-hexenoic acid,

- 25 N, β , β -Trimethyl-L-phenylalanyl- N^1 -[(1S,2E)-3-carboxy-1-isopropyl-2-pentenyl]- N^1 ,3-dimethyl-L-valinamide,

Ethyl (E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-(methylsulfanyl)butanoyl]amino}-2-hexenoate,

- 30 (E,4S)-2,5-dimethyl-4-{methyl[(2R)-3-methyl-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}-3-(methylsulfanyl)butanoyl]amino}-2-hexenoic acid,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-3-(methylsulfonyl)-L-valinamide,

5 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-3-[(4-methoxybenzyl)sulfanyl]-N¹-methyl-L-valinamide,

N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-3-[(4-methoxybenzyl)sulfanyl]-N¹-methyl-L-valinamide and

10 N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-3-(methylsulfonyl)-L-valinamide
or pharmaceutically acceptable salts thereof.

43. The method according to claim 28 wherein said compound of Formula (II) is
15 selected from:

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1R,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-but enyl]-N¹-methyl-L-allothreoninamide,

20 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-allothreoninamide,

N, β , β -trimethyl-L-phenylalanyl-N-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N,O, β , β -tetramethyl-L-tyrosinamide,

25 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,O-dimethyl-L-allothreoninamide,

30 (E,4S)-2,5-Dimethyl-4-[methyl((2S)-2-{{(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl}amino}-4-phenylbutanoyl)amino]-2-hexenoic acid,

N, β , β -trimethyl-L-phenylalanyl-4-benzoyl-N-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]- N, β , β -trimethyl-L-phenylalaninamide and

4-benzoyl-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide
or pharmaceutically acceptable salts thereof.

5

44. The method according to claim 28 wherein said compound of Formula (II) is selected from:

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-N¹-methyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isobutylbut-2-enyl]-3-methyl-L-valinamide,

15 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-ethyl-3-methyl-L-valinamide,

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-ethyl-L-valinamide,

20

N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-methyl-L-leucinamide,

25 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹-methyl-L-norvalinamide,

(2E,4S)-4-[{(2R)-2-cyclohexyl-2-[(N, β,β -trimethyl-L-phenylalanyl)amino]ethanoyl}(methyl)amino]-2,5-dimethylhex-2-enoic acid,

30 (2E,4S)-2,5-dimethyl-4-(methyl{(2S)-2-[(N, β,β -trimethyl-L-phenylalanyl)amino]butanoyl}amino)hex-2-enoic acid,

4-{{[3,3-Dimethyl-2-(2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino}-2,5-dimethyl-hex-2-enoic acid,

5 N, β,β-trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-methyl-L-valinamide,

N, β,β-trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-L-valinamide,

10 2,5-dimethyl-4-{methyl-[2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-propionyl]-amino}-hex-2-enoic acid,

4-{{[3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]-methyl-amino}-2,6-dimethyl-hept-2-enoic acid,

15 N, β,β-trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-valinamide and

N, β,β-trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹-methyl-L-isoleucinamide
20 or pharmaceutically acceptable salts thereof.

45. The method according to claim 28 wherein said compound of Formula (II) is selected from:

25 (E,4S)-4-[((2S)-3,3-dimethyl-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)(methyl)amino]-2,5-dimethyl-2-hexenamide,

(E,4S)-4-[((2S)-3,3-dimethyl-2-[(2S)-3-methyl-2-(methylamino)-3-phenylbutanoyl]amino}butanoyl)(methyl)amino]-N,2,5-trimethyl-2-hexenamide,
30

N, β,β-trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(2-cyanoethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-but enyl}-N¹,3-dimethyl-L-valinamide,

- N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(carboxymethyl)amino]-1-isopropyl-3-methyl-4-oxo-2-but enyl}-N¹,3-dimethyl-L-valinamide,
- 5 N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[(4-azidophenyl)amino]-1-isopropyl-3-methyl-4-oxo-2-but enyl}-N¹,3-dimethyl-L-valinamide,
- N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-[(2-phenylethyl)amino]but-2-enyl}-N¹,3-dimethyl-L-valinamide,
- 10 N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[[((1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxobut-2-enyl)(methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl}-N¹,3-dimethyl-L-valinamide,
- 15 N, β,β -trimethyl-L-phenylalanyl-N¹-{(1S,2E)-4-[[((1S,2E)-3-carboxy-1-isopropylbut-2-enyl)(methyl)amino]-1-isopropyl-3-methyl-4-oxobut-2-enyl}-N¹,3-dimethyl-L-valinamide,
- N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-isopropyl-3-methyl-4-oxo-4-(thien-2-ylmethoxy)but-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 20 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-isopropyl-3-methyl-4-(octyloxy)-4-oxobut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 25 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2Z)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide and
N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylprop-2-enyl]-N¹,3-dimethyl-L-valinamide
- 30 or pharmaceutically acceptable salts thereof.

46. The method according to claim 28 wherein said compound of Formula (II) is selected from:

- N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-1-allyl-3-carboxybut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,
- (2E,4S)-4-[{(2S)-3,3-dimethyl-2-[(N, β,β -trimethyl-L-phenylalanyl)amino]-4-pentenoyl}(methyl)amino]-2,5-dimethyl-2-hexenoic acid,
- 10 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-isoleucinamide,
- N, β,β -trimethyl-L-phenylalanyl-N¹-[(1R,3S)-3-carboxy-1-isopropylbutyl]-N^{1,3}-dimethyl-L-valinamide,
- 15 N, β,β -trimethyl-L-phenylalanyl-N¹-[(1R,3R)-3-carboxy-1-isopropylbutyl]-N^{1,3}-dimethyl-L-valinamide,
- β,β -diethyl-N-methyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,
- 20 N^{1,3}-dimethyl-L-valinamide,
- β,β -diethyl-N-methyl-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide,
- 25 (betaS)-N,beta-dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide and
O-benzyl-N-methyl-L-threonyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N^{1,3}-dimethyl-L-valinamide
- 30 or pharmaceutically acceptable salts thereof.

47. The method according to claim 28 wherein said compound of Formula (II) is selected from:

3-Cyclohexyl-N-methyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-

5 N¹,3-dimethyl-L-valinamide and

3-cyclohexyl-N-methyl-L-valyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2- butenyl]-N¹,3-dimethyl-L-valinamide

or pharmaceutically acceptable salts thereof.

10

48. The method according to claim 28 wherein said compound of Formula (II) is selected from:

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-2-(methylamino)-2-(1-

15 phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2R)-2-(methylamino)-2-(1- phenylcyclopropyl)acetyl]-L-valyl}amino)hex-2-enoic acid,

20 2-(4-{[3,3-Dimethyl-2-(3-methyl-2-methylamino-3-phenyl-butyrylamino)-butyryl]- methyl-amino}-2,5-dimethyl-hex-2-enoylamino)-4-methylsulfanyl-butyric acid methyl ester,

N, β , β -trimethyl-L-phenylalanyl-N1-((1S,2E)-4-[(1S)-1-carboxy-3-

25 (methylthio)propyl]amino}-1-isopropyl-3-methyl-4-oxobut-2-enyl)-N1,3-dimethyl-L- valinamide,

N, β , β -trimethyl-4-[(E)-2-phenylvinyl]-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

30

N, β , β -trimethyl-4-[(E)-2-phenylvinyl]-D-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1- isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N¹-methyl-D-valinamide,

5 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-fluoro-N¹-methyl-L-valinamide,

3-[(4-methoxybenzyl)thio]-N-methyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

10 N-ethyl- β , β -dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

(2E,4S)-2,5-dimethyl-4-(methyl{3-methyl-N-[(2S)-3-methyl-3-phenyl-2-pyrrolidin-1-ylbutanoyl]-L-valyl}amino)hex-2-enoic acid,

15 N-(2-hydroxyethyl)- β , β -dimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

(β R)-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

20 3-acetyl-N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

25 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-3-hydroxy-N¹-methyl-L-valinamide and

N, β , β -trimethyl-L-phenylalanyl-N¹-[(1R,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide.

30 or pharmaceutically acceptable salts thereof.

49. The method according to claim 28 wherein said compound of Formula (II) is selected from:

- 5 3-Chloro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 10 3-bromo-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,
- 15 N, β,β ,3-Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 20 3-Cyclohexyl-N-methyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 25 N,O, β,β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,
- 30 N,O, β,β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,methyl-3-(methylsulfanyl)-L-valinamide, and
- 35 N, β,β -3,4-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide.
- 40 50. The method according to claim 28 wherein said compound of Formula (II) is N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide.
- 45 51. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of a compound selected from the group:

3-Chloro-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

5 3-bromo-N, β,β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide,

N, β,β ,3-Tetramethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

10 3-Cyclohexyl-N-methyl-L-valyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

N,O, β,β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹,3-dimethyl-L-valinamide,

15 N,O, β,β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-butenyl]-N¹-methyl-3-(methylsulfanyl)-L-valinamide, and

20 N, β,β -3,4-Pentamethyl-L-phenylalanyl-N¹-[(1S,2E)-4-ethoxy-1-isopropyl-3-methyl-4-oxo-2-butenyl]-N¹,3-dimethyl-L-valinamide

or a pharmaceutically acceptable salt thereof.

25 52. The method according to Claim 51 wherein the chemotherapeutic agents are antimicrotubule inhibitors.

53. The method according to Claim 52 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine and vinorelbine.

30 54. The method according to claim 51 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia,

kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

55. The method according to Claim 51 wherein the tumors overexpress MDR-1,
5 MXR or MRP.
56. The method according to Claim 51 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).
- 10 57. The method according to Claim 51 wherein the resistance is inherent or acquired.
58. The method according to Claim 57 wherein the resistance is acquired.
- 15 59. The method according to Claim 51 wherein a compound is administered before, concurrently, or after treatment with the chemotherapeutic agent.
60. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of the compound
20 N, β , β -trimethyl-L-phenylalanyl-N¹-[(1S,2E)-3-carboxy-1-isopropylbut-2-enyl]-N¹,3-dimethyl-L-valinamide or a pharmaceutically acceptable salt thereof.
- 25 61. The method according to Claim 60 wherein the chemotherapeutic agents are antimicrotubule inhibitors.
62. The method according to Claim 61 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine and vinorelbine.
30
63. The method according to claim 60 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia,

kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

64. The method according to Claim 60 wherein the tumors overexpress MDR-1,
5 MXR or MRP.

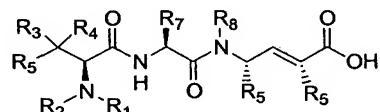
65. The method according to Claim 60 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).

10 66. The method according to Claim 60 wherein the resistance is inherent or acquired.

67. The method according to Claim 66 wherein the resistance is acquired.

15 68. The method according to Claim 60 wherein the compound is administered before, concurrently, or after treatment with the chemotherapeutic agent.

69. A process for the preparation of a carboxylic acid of the formula



20

wherein:

R₁ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

25
30

R_2 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, NO₂, -SO₃H, -SOR₁₀ or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

5 or R₁ and R₂ taken together with the nitrogen atom to which they are attached is a three to seven membered ring;

10

R_3 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

15

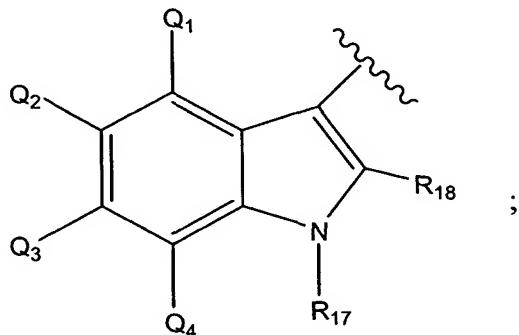
20 R_4 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

25

30 or R₃ and R₄ taken together with the carbon to which they are attached form a three to seven membered ring;

R_5 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R- and aryl and provided that when R₅ is an indolyl moiety of the formula

10



R_{17} is H or an optionally substituted alkyl or acyl group; and
 R_{18} Q₁, Q₂, Q₃ and Q₄ are independently selected from H, halogen, alkyl, acyl,
15 -OH, -O-alkyl, -O-acyl, -NH₂, -NH-alkyl, -N(alkyl)₂, -NH-acyl, -NO₂, -SH, -S-alkyl and
-S-acyl, wherein the alkyl and acyl groups of the substituents are optionally
substituted;

R_7 is selected from the group consisting of a saturated or unsaturated moiety
20 having a linear, branched, or cyclic skeleton containing one to ten carbon atoms,
zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms,
said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀,
-SH, -SR₁₀, -SOCR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F,
-CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH,
25 -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or
cyclic, one to ten carbon saturated or unsaturated alkyl group; and
aryl-R-;

R_8 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and

10 aryl-R-;

and wherein,

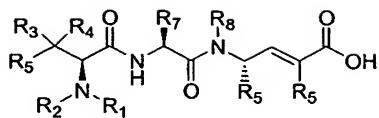
R is a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group;

X is a moiety selected from the group consisting of -OH, -OR, =O, =S, -O₂CR, -SH, -SR, -SO₂CR, -NH₂, -NHR, -N(R)₂, -NHCOR, NRCOR, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R, -CHO, -COR, -CONH₂, -CONHR, -CON(R)₂, -COSH, -COSR, -NO₂, -SO₃H, -SOR, and -SO₂R;

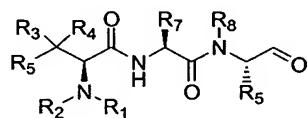
Aryl is an aromatic ring selected from the group consisting of: phenyl, naphthyl, anthracyl, phenanthryl, thienyl, furyl, indolyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and pyridyl, optionally substituted with R or X;

comprising the steps of:

a) treating a carboxylic acid of the formula

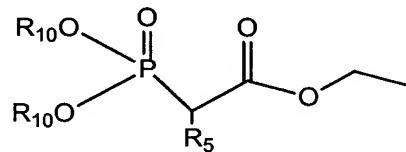


with ozone in the methanol followed by further treating with
5 dimethylsulfide to obtain an aldehyde of the formula



10

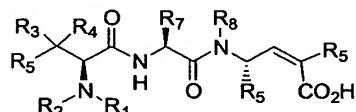
b) reacting said aldehyde with a phosphonate of the formula



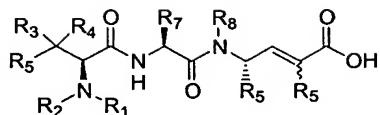
15

where R₁₀ is optionally fluoro substituted alkyl of 1 to 10 carbon atoms,
in the presence of potassium hexamethyldisilazide and 18-crown-6 and hydrolyzing
with base to obtain a carboxylic acid of the formula

20



70. A process for the preparation of a carboxylic acid of the formula



wherein:

- R₁ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;
- 10

- R₂ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, -CO₂H, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, NO₂, -SO₃H, -SOR₁₀ or -SO₂R₁₀, wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;
- 15
- or R₁ and R₂ taken together with the nitrogen atom to which they are attached is a three to seven membered ring;
- 20

- R₃ is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;
- 25

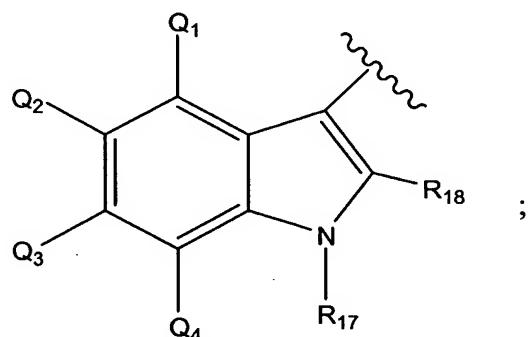
R_4 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀,

- 5 -O₂CR₁₀, -SH, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

10

or R₃ and R₄ taken together with the carbon to which they are attached form a three to seven membered ring;

- 15 R_5 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R- and aryl and provided that when R₅ is an indolyl moiety of the formula



25

R₁₇ is H or an optionally substituted alkyl or acyl group; and

R_{18} , Q_1 , Q_2 , Q_3 and Q_4 are independently selected from H, halogen, alkyl, acyl, -OH, -O-alkyl, -O-acyl, -NH₂, -NH-alkyl, -N(alkyl)₂, -NH-acyl, -NO₂, -SH, -S-alkyl and -S-acyl, wherein the alkyl and acyl groups of the substituents are optionally substituted;

5

R_7 is selected from the group consisting of a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

15

R_8 is selected from the group consisting of H; a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group; and aryl-R-;

25

and wherein,

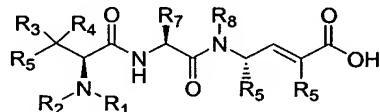
R is a saturated or unsaturated moiety having a linear, branched, or cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, said carbon atoms being optionally substituted with: =O, =S, OH, -OR₁₀, -O₂CR₁₀, -SH, -SR₁₀, -SO₂CR₁₀, -NH₂, -NR₁₀H, -N(R₁₀)₂, -NHCOR₁₀, -NR₁₀COR₁₀, -I, Br, -Cl, -F, -CN, CO₂H, -CO₂R₁₀, -CHO, -COR₁₀, -CONH₂, -CONHR₁₀, -CON(R₁₀)₂, -COSH, -COSR₁₀, -NO₂, -SO₃H, -SOR₁₀, or -SO₂R₁₀,

-SO₂R₁₀ wherein R₁₀ is a linear, branched or cyclic, one to ten carbon saturated or unsaturated alkyl group;

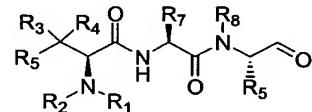
- X is a moiety selected from the group consisting of -OH, -OR, =O, =S,
 5 -O₂CR, -SH, -SR, -SO₂CR, -NH₂, -NHR, -N(R)₂, -NHCOR, NRCOR, -I, Br, -Cl, -F, -CN, -CO₂H, -CO₂R, -CHO, -COR, -CONH₂, -CONHR, -CON(R)₂, -COSH, -COSR, -NO₂, -SO₃H, -SOR, and -SO₂R;

- Aryl is an aromatic ring selected from the group consisting of: phenyl,
 10 naphthyl, anthracyl, phenanthryl, thienyl, furyl, indolyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and pyridyl, optionally substituted with R or X;

- comprising the steps of:
 15 b) treating a carboxylic acid of the formula

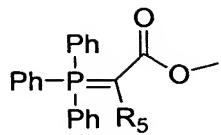


- with ozone in methanol followed by further treating with dimethylsulfide to obtain an
 20 aldehyde of the formula

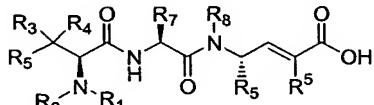


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- c) reacting said aldehyde of step a) with triphenylphosphorane of the formula



and hydrolyzing with base to obtain said carboxylic acid having the formula



71. The process according to Claim 69 wherein the base in step b) is aqueous lithium hydroxide.

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72. The process according to Claim 70 wherein the base in step b) is aqueous lithium hydroxide.

15

73. A method of treating, inhibiting the growth of, or eradicating a tumor in a mammal in need thereof wherein said tumor is resistant to at least one chemotherapeutic agent which method comprises providing to said mammal an effective amount of the compound

N,O, β , β -tetramethyl-L-tyrosyl-N¹-[(1S,2E)-3-carboxy-1-isopropyl-2-but enyl]-N¹,3-dimethyl-L-valinamide.

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74. The method according to Claim 73 wherein the chemotherapeutic agents are antimicrotubule inhibitors.

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75. The method according to Claim 74 wherein the antimicrotubule inhibitors are selected from the group consisting of paclitaxel, docetaxel, vinblastine, vincristine and vinorelbine.

76. The method according to Claim 73 wherein the tumors are selected from the group consisting of breast, colon, lung, prostate, melanoma, epidermal, leukemia,

kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin and brain.

77. The method according to Claim 73 wherein the tumors overexpress MDR-1,

. 5 MXR or MRP.

78. The method according to Claim 73 wherein the resistance to chemotherapeutic agents is multiple drug resistance (MDR).

10 79. The method according to Claim 73 wherein the resistance is inherent or acquired.

80. The method according to Claim 79 wherein the resistance is acquired.

15 81. The method according to Claim 73 wherein the compound is administered before, concurrently, or after treatment with the chemotherapeutic agent.